

We claim:

1. An improved method for manufacturing delivery devices for the transdermal administration of a liquid drug capable of forming a crystalline structure,
5 the method comprising:
 - a) heating, to a predetermined temperature, each individual film or laminate of a transdermal delivery device which comprises a dispersion of said liquid drug in a matrix immediately following film formation or lamination;
 - b) maintaining each film or laminate at the desired temperature for
10 a period of time sufficient to prevent the formation and/or growth of a crystalline structure in any film or laminate; and
 - c) allowing each film or laminate to cool to ambient conditions.
2. The method according to claim 1 further comprising the step of
15 providing that each dispersion of said liquid drug in a matrix is placed between two non-porous substrates prior to heating.
3. The method according to claim 2 further comprising the steps of:
 - c) laminating the individual films or laminates to form a final
20 laminate ;
 - d) heating the final laminate to said predetermined temperature immediately following lamination and maintaining the final laminate at the temperature for a period of time sufficient to prevent formation and/or growth of a crystalline structure in the final laminate; and
 - 25 e) allowing the final laminate to cool to ambient conditions.
4. The method according to claim 3 further comprising the steps of:
 - e) cutting subunits from said final laminate and forming said
delivery devices;
 - 30 f) packaging said delivery devices in sealed containers;
 - g) heating the devices in said containers to a predetermined temperature and maintaining the devices at the temperature for a period of time

sufficient to prevent formation and/or growth of a crystalline structure in the devices;
and

h) allowing the sealed devices to cool to ambient conditions.

5 5. The method according to claim 3 wherein the predetermined temperature is above the melting point of the crystalline structure and the period of time is sufficient to melt any crystals present in the dispersion.

10 6. The method according to claim 1 wherein the device comprises an impermeable backing lamina, a drug reservoir layer, a release rate controlling layer, and adhesive layer, and a release liner layer and said dispersion forms said drug reservoir layer.

15 7. The method of claim 6 wherein the dispersion forms said adhesive layer.

8. The method of claim 2 wherein the drug is scopolamine.

20 9. The method of claim 8 wherein the predetermined temperature is within the range of 75-90° C and the period of time is 2-10 minutes.

25 10. The method of claim 4 wherein the liquid drug is scopolamine and the devices sealed within the containers are heated to a temperature of about 75° C for a period of approximately 4 - 24 hours.

11. A process for preventing the formation of the crystalline structure of a liquid drug dispersed within a matrix which comprises:

30 a) forming a laminate wherein each individual film or lamina comprising a dispersion of said liquid drug in a matrix is heated to a predetermined temperature immediately following formation or lamination;

b) maintaining each film or lamina at the desired temperature for a period of time sufficient to prevent the formation and/or growth of a crystalline structure in any film or lamina; and

c) allowing each film or lamina to cool to ambient conditions.

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12. A process according to claim 11 further comprising the step of providing that each dispersion of said liquid drug in a matrix is placed between two non-porous substrates prior to heating.

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13. A process according to claim 12 wherein the predetermined temperature is above the melting point of the crystalline structure and the period of time is sufficient to melt any crystals present in the dispersion.

14. An improved method of manufacturing delivery devices for the transdermal administration of a liquid drug capable of forming a crystalline structure, comprising:

a) forming a drug reservoir / backing film, said drug reservoir comprising a liquid drug capable of forming a crystalline structure;

b) immediately following forming the drug reservoir / backing film, performing a first annealing step wherein the drug reservoir / backing film is heated to a predetermined temperature for a period of time sufficient to prevent formation and/or growth of a crystalline structure and thereafter allowed to cool to ambient conditions;

c) forming a contact adhesive / release liner film, said contact adhesive comprising a liquid drug capable of forming a crystalline structure;

d) immediately following forming the contact adhesive / release liner film, performing a second annealing step wherein the contact adhesive / release liner film is heated to a predetermined temperature for a period of time sufficient to prevent formation and/or growth of a crystalline structure and thereafter allowed to cool to ambient conditions;

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e) laminating the drug reservoir surface of the drug reservoir / backing film to the contact adhesive surface of the contact adhesive / release liner film to form a final laminate;

f) immediately following forming the final laminate, performing a
5 third annealing step wherein the final laminate is heated to a predetermined temperature and maintaining the temperature for a period of time sufficient to prevent the formation and/or growth of a crystalline structure in the final laminate and thereafter allowing the final laminate to cool to ambient conditons.

10 15. The method according to claim 14 further comprising the steps of:

placing a non-porous substrate on the drug reservoir surface of said drug reservoir / backing film prior to said first annealing step;

placing a non-porous substrate on the contact adhesive surface of said contact adhesive / release liner laminate prior to said second annealing step;

15 and

removing the non-porous substrates from said drug reservoir / backing film and said contact adhesive / release liner film prior to laminating the drug reservoir surface of the drug reservoir / backing film to the contact adhesive surface of the contact adhesive / release liner film to form the final laminate.

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16. The method according to claim 15 wherein the predetermined temperature is above the melting point of the crystalline structure and the period of time is sufficient to melt any crystals present in the dispersion.

25 17. The method according to claim 16 further comprising the steps of:

cutting subunits from said final laminate and forming said delivery devices;

packaging said delivery devices in sealed containers;

heating the devices in said containers to a predetermined
30 temperature and maintaining the devices at the temperature for a period of time sufficient to prevent formation and/or growth of a crystalline structure in the devices;
and

allowing the sealed devices to cool to ambient conditions.

18. The method according to claim 14 further comprising the step of laminating a rate control membrane to the contact adhesive surface of the contact
5 adhesive / release liner film to form a rate control membrane / contact adhesive / release liner laminate prior to said second annealing step.

19. The method according to claim 18 further comprising the steps of
placing a non-porous substrate on the drug reservoir
10 surface of said drug reservoir / backing film prior to said first annealing step;
placing a non-porous substrate on the surface of the rate control membrane prior to said second annealing step; and
removing the non-porous substrates from said drug reservoir /
backing film and said rate control membrane / contact adhesive / release liner
15 laminate; and
laminating the drug reservoir surface of the drug reservoir /
backing film to the surface of the rate control membrane of the rate control
membrane / contact adhesive / release liner laminate to form the final laminate.

20. 20. The method according to claim 19 wherein the predetermined
temperature is above the melting point of the crystalline structure and the period of
time is sufficient to melt any crystals present in the dispersion.

21. The method according to claim 20 further comprising the steps of:
25 cutting subunits from said final laminate and forming said
delivery devices;
packaging said delivery devices in sealed containers;
heating the devices in said containers to a predetermined
temperature and maintaining the devices at the temperature for a period of time
30 sufficient to prevent formation and/or growth of a crystalline structure in the devices;
and
allowing the sealed devices to cool to ambient conditions.

22. The method according to claim 18 wherein the rate control membrane is a microporous polypropylene membrane saturated with mineral oil.

5 23. The method according to claim 21 wherein the liquid drug is scopolamine base.

24. The method according to claim 23 wherein the predetermined temperature in the first, second, and third annealing steps is approximately 75-90° C
10 and the period of time is about 2-10 minutes.

25. The method according to claim 24 wherein the devices sealed within the containers are heated to a temperature of about 75° C for a period of approximately 4-24 hours.

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26. A drug delivery device for the transdermal administration of scopolamine manufactured by the method according to any one of claims 1, 14, or 25.

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